

The University of Chicago

Founded by JOHN D. ROCKEFELLER

On the Molecular Rearrangement of
o-Aminophenylethyl Carbonate to
o-Oxyphenylurethane

A DISSERTATION

SUBMITTED TO THE FACULTIES OF THE GRADUATE SCHOOLS
OF ARTS, LITERATURE, AND SCIENCE, IN CANDIDACY
FOR THE DEGREE OF DOCTOR OF PHILOSOPHY

DEPARTMENT OF CHEMISTRY

By JAMES H. RANSOM

EASTON, PA.:
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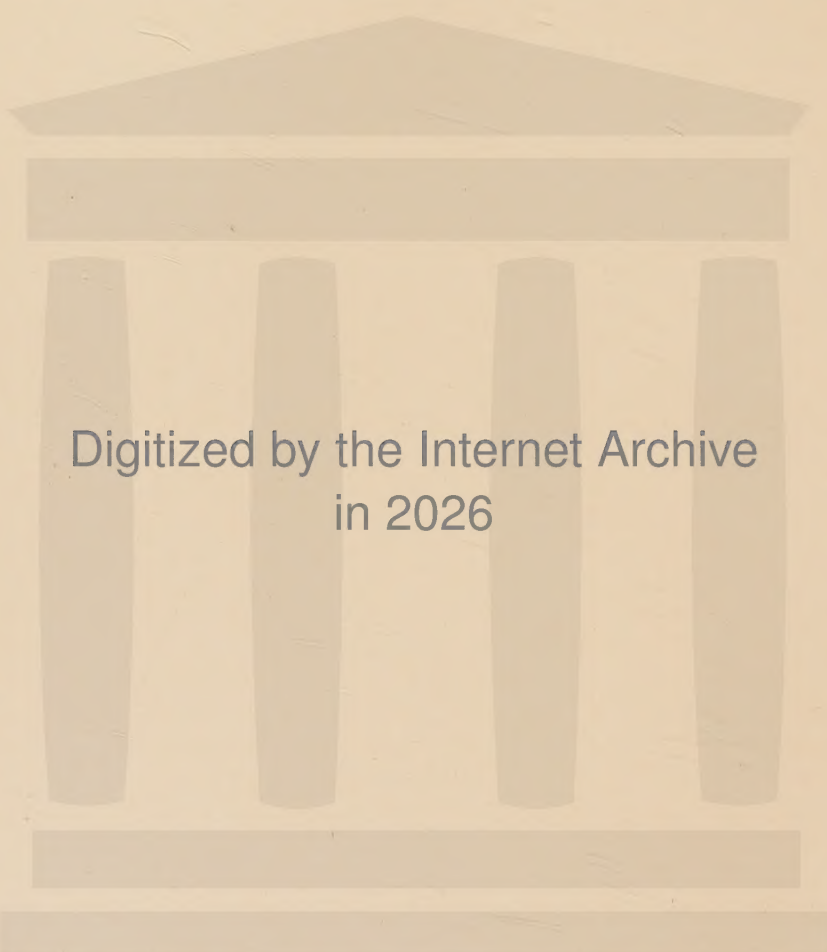


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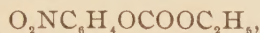


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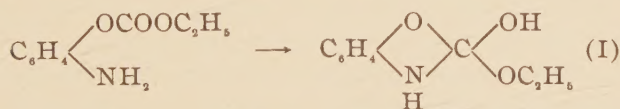
On the Molecular Rearrangement of *o*-Aminophenylethyl Carbonate to *o*-Oxyphenylurethane.¹

BY JAMES H. RANSOM.

On reducing *o*-nitrophenylethyl carbonate,



with tin and hydrochloric acid in alcoholic solution, according to Bender,² a white crystalline compound (melting-point 95°, as given by Bender) separates out of the acid solution. Analysis gave figures agreeing with the composition of the expected reduction-product, aminophenylethyl carbonate, $\text{H}_2\text{NC}_6\text{H}_4\text{OCOOC}_2\text{H}_5$, and this constitution has been ascribed to the compound in spite of the striking absence of basic properties. The seeming contradiction between properties and constitution led Professor Stieglitz, who recently had occasion to use the substance in connection with an investigation with Dr. H. N. McCoy,³ to suspect that after the reduction of the nitro compound to an amine base, a molecular rearrangement of the latter produces Bender's body. Such a molecular rearrangement could occur in one of the following ways :



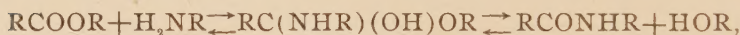
¹ See a preliminary report : Ber. d. chem. Ges., **31**, 1055.

² Ber. d. chem. Ges., **19**, 2268.

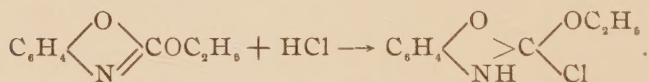
³ Am. Chem. J., **21**, 111.



The well-known ease with which *o*-aminophenols give ring compounds suggested constitution (I). The possibility of isolating and identifying a substance of such a constitution seemed particularly important and worthy of close investigation for two reasons. In the first place, in the action of amines on acid esters, and *vice versa*, of alcohols on acid amides, an intermediate addition-product is quite generally assumed to be formed according to



but the addition-product has not been isolated. Formula (I) represents such an addition-product of an amine to an ester, made stable, possibly, by the general tendency towards the formation of ortho rings. In the second place formula (I) represents the constitution of the hydroxide base corresponding to the hydrochloride of ethoxymethenylaminophenol (an imido ether) if the salts of imido ethers are formed by the addition of the acid to the double bond between the carbon and nitrogen atoms :¹



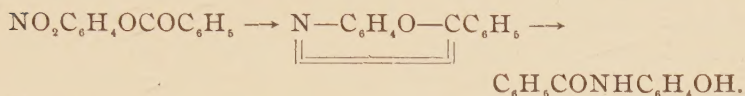
A substance of constitution (I) would have to show the most intimate relationship to this hydrochloride; and the existence or non-existence of such a relationship would go a great way towards settling the constitution of the hydrochlorides of imido ethers.

Constitution (II) would result from the migration of an acyl group from a negative phenol radical to the basic amido group. Similar migrations have been observed, occasionally, before. Notably *o*-nitrophenyl benzoate, closely related to the nitro body under investigation, gives on reduction in hot alcoholic solution benzoyl-*o*-aminophenol. Böttcher² showed

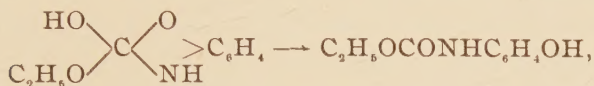
¹ *Vide* Stieglitz: Am. Chem. J., 21, 101.

² Ber. d. chem. Ges., 16, 630.

that the anhydro base, benzenylaminophenol, is formed by loss of water in the experiment, and under the same conditions goes over into benzoylaminophenol by the addition of water :



He concluded, therefore, that benzenylaminophenol is an intermediate product in the rearrangement. But a substance of formula (II) could result, without the formation of an anhydro base, by further transformation of (I), according to



a change entirely analogous to the conversion of an acid ester into an acid amide, as shown on page 12.

Such a rearrangement of an aminophenyl carbonate into an oxyphenylurethane (II), demonstrated to occur only in the ortho series, and to take place without the intermediate formation of an anhydro base, would prove the intermediate formation of compound (I), and thus incidentally strongly support the modern conception of ester and amide transformations. In such an event, also, the substance of constitution (I) would be shown to have an existence, however, transitory, and it might be possible to establish, even then, some connection between it and the hydrochloride of ethoxymethenylaminophenol, although the inability to isolate the hydroxide itself would, no doubt, render such a work not only more difficult but also far less decisive in determining the constitution of the hydrochlorides of the imido ethers.

With these objects in view, the present investigation was suggested by, and carried out under the direction of, Professor Stieglitz, to determine first, the true constitution of the reduction-product of *o*-nitrophenylethyl carbonate (Bender's compound), that no opportunity might pass for isolating and investigating a possible hydroxide of constitution (I), and

secondly, to study more closely than has been done by Böttcher and others the mechanism of the rearrangement after reduction.

The facts bearing on the question of the constitution of Bender's compound (m. p. 95°) known at the outset of this investigation were as follows: It crystallized out of strong acid solution and could not possibly have the constitution $\text{H}_2\text{NC}_6\text{H}_4\text{OCOOC}_2\text{H}_5$, which he assigned to it. Such a substance would have approximately the basicity of aniline and would dissolve readily in dilute hydrochloric acid (as has since been confirmed by isolating aminophenylethyl carbonate).

On the other hand, Bender prepared an acetyl derivative of his compound that on distilling gave acetylcarbonylamino-phenol¹, $\text{CH}_3\text{CO}-\text{N}-\text{C}_6\text{H}_4-\text{O}-\text{C}=\text{O}$, which evidently is in

$$\begin{array}{c} \text{CH}_3\text{CONHC}_6\text{H}_4\text{OCOOC}_2\text{H}_5 \\ \text{—————} \end{array}$$

better accord with Bender's view of the constitution, $\text{CH}_3\text{CONHC}_6\text{H}_4\text{OCOOC}_2\text{H}_5$, than, for instance, with the isomeric constitution, $\text{CH}_3\text{COOC}_6\text{H}_4\text{NHCOOC}_2\text{H}_5$. Finally Groenvik² had already prepared an oxyphenylurethane (II), $\text{HOC}_6\text{H}_4\text{NHCOOC}_2\text{H}_5$ (soluble in alkalis, insoluble in dilute acids), from *o*-aminophenol and ethyl chlorformate, and found its melting-point to be 85° , which is 10° lower than that of Bender's compound. On comparing the two substances I found them to be identical. After one or more recrystallizations, of preparations made a number of times, the melting-point of both bodies was found to be 86° ,³ and this was not changed by mixing the two compounds even without recrystallizing. Both dissolve easily in alkalis and give in alkaline solution the same benzoate. In view of the solubility of the substance in alkali no doubt can remain that Bender's compound was not an aminophenylethyl carbonate but had suffered molecular rearrangement to (I) or (II).

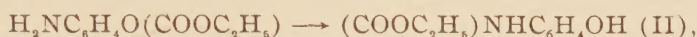
On reducing *o*-nitrophenylethyl carbonate, *o*-aminophenylethyl carbonate is undoubtedly first formed. The acid solu-

¹ Bender: Ber. d. chem. Ges., **19**, 2270.

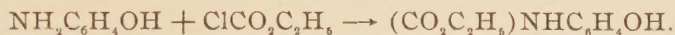
² Bull. Soc. Chim., **25**, 177.

³ The melting-point given by Bender is probably due to a typographical error or to an unreliable thermometer: *Vide*, Ber. d. chem. Ges., **19**, 2951.

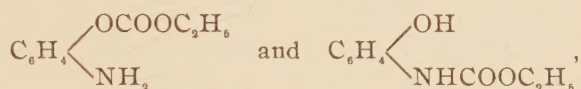
tion remains clear for some time, and the precipitation of Bender's compound is completed, in the cold, only after a day or two. By keeping the solution very cold while reducing and then rendering immediately alkaline, and extracting with ether, I was able to isolate *o*-aminophenylethyl carbonate—an oil soluble in dilute acids but insoluble in alkali—as the product of the first stage of the reaction. In the acid solution, therefore, a rearrangement of aminophenylethyl carbonate to oxyphenylurethane must occur according to



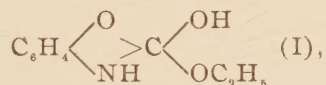
if Groenvik's oxyphenylurethane really has the constitution one would be inclined to assign to it on the basis of its solubility in alkalis and of its preparation from *o*-aminophenol and ethyl chlorformate :



It is obvious, however, that the attempt to prepare two compounds,



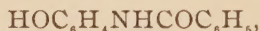
could also lead to one and the same body, if in both cases the well-known tendency of the ortho series to form ring compounds was exhibited—both substances could yield the ring compound,



as the stable form. It still remained, therefore, to determine whether *o*-oxyphenylurethane has the constitution (I) or (II).

The attempt to decide this question by alkylating with methyl iodide in alkaline solution was quite unsuccessful. Most of the substance was recovered unchanged. The substance also proved to be too sensitive to the oxidizing effects of silver oxide to prepare a silver salt for the purpose of methylation (blackening occurred under all conditions).

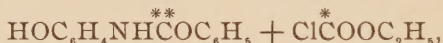
On the other hand, acyl derivatives were so easily made in the cold, by Baumann's method, with quantitative yields, that this method of investigation was pursued next. It led to most surprising results, the experimental data of which were carefully confirmed by me by two independent investigations with an interval of half a year. By benzoylating oxyphenylurethane, as Bender's and Groenvik's compound may be called, a benzoyl derivative is obtained melting at $75^{\circ}.5$. If oxyphenylurethane has the constitution its name expresses (II), the benzoate should be $C_6H_5COOC_6H_4NHCOOC_2H_5$. But exactly the same benzoyloxyphenylurethane (m. p. $75^{\circ}.5$) was obtained by me on treating benzoyl-*o*-aminophenol,



(from *o*-aminophenol and benzoyl chloride; soluble in alkalis, insoluble in acids), in alkaline solution with ethyl chlorformate. Both bodies melt at $75^{\circ}.5$ and there is no depression of the melting-point on mixing them. The two reactions,

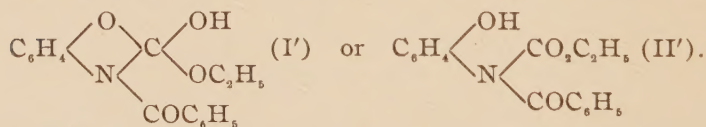


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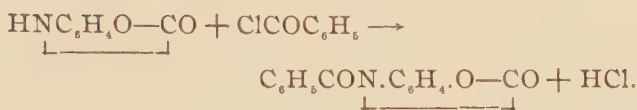
give the same product. The inevitable conclusion (excluding molecular rearrangements) is that both acyl carbon atoms,

^{*}C and ^{**}C, must be attached to the nitrogen atom in benzoyloxyphenylurethane. The latter would then be



The behavior of benzoyloxyphenylurethane towards heat would seem to show that, when oxyphenylurethane is benzoylated, the benzoyl group goes to the nitrogen atom. On heating it gives alcohol and benzoylcarbonylaminophenol,¹ in which the benzoyl group is found attached to nitrogen. The same substance was obtained by benzoylating carbonylaminophenol:

¹ Bender's acetaminophenylethyl carbonate shows similar behavior.



Benzoyloxyphenylurethane is insoluble in alkalies and shows none of the properties of a phenol. An acyl group entering the urethane molecule according to



would be without a parallel under the conditions observed. Phenylurethane, *o*-methoxyphenylurethane, etc., are not benzoylated under the same conditions. Consequently formula (II') can be considered as completely disposed of as a possible constitution for benzoyloxyphenylurethane. If both acyl

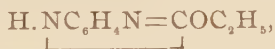
carbon atoms ^{*}C and ^{**}C are attached to nitrogen only formula (I') would be left to represent the true constitution of benzoyloxyphenylurethane, and oxyphenylurethane itself would have the ring constitution



Imide groups in similar ring complexes have frequently been found to give to compounds acid properties. For instance, ethenyl-*o*-phenylenediamine,¹



and ethoxymethenyl-*o*-phenylenediamine,²



are soluble in alkalies, and this is undoubtedly due to the presence of the imide group (NH) in these substances. The solubility, in alkalies, of oxyphenylurethane as a ring derivative could then very well be due to the imide group, and, on benzoylating such a compound, the union of the benzoyl group with the nitrogen atom, as found above, would be expected in a normal case. The behavior of oxyphenylureth-

¹ Bamberger: Ann. Chem. (Liebig), **273**, 274.

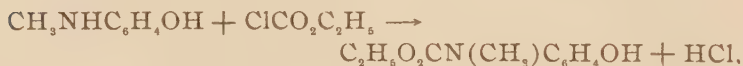
² Sandmeyer: Ber. d. chem. Ges., **19**, 2654.

ane towards acyl chlorides—exactly the same results were obtained on using *m*-nitrobenzoyl chloride in place of benzoyl chloride—agrees in every detail far better, therefore, with constitution (I), $\text{HNC}_6\text{H}_4\text{OC}(\text{OH})\text{OC}_2\text{H}_5$, than with consti-

tution (II), $\text{HOC}_6\text{H}_4\text{NHCO}_2\text{C}_2\text{H}_5$.¹

But in view of the fact that we were dealing with derivatives, for which one molecular rearrangement of the mother substance had already been positively proved, these conclusions were further tested as follows: Benzoyloxyphenylurethane, as $(\text{C}_6\text{H}_5\text{CO})\text{N}.\text{C}_6\text{H}_4\text{OC}(\text{OH})\text{OC}_2\text{H}_5$, being insoluble in

alkalies, the alcoholic hydroxyl group could have no marked acid properties. Now oxyphenylmethylurethane can be prepared from methylaminophenol and ethyl chlorformate according to the equation:



and being in every way analogous to oxyphenylurethane, it must have an analogous constitution, and would be, as a ring derivative, $\text{CH}_3\text{NC}_6\text{H}_4\text{OC}(\text{OH})\text{OC}_2\text{H}_5$. Such a compound, as

explained in the case of benzoyloxyphenylurethane, having no acid imide group, should have no marked acid properties. On preparing oxyphenylmethylurethane it was found to dissolve quite readily in alkalies like an ordinary phenol. This result made the ring constitution for it, and consequently for oxyphenylurethane itself, again very doubtful, since the surprising nature of the acyl derivatives—verified experimentally in every point again—could very well be due to molecular rearrangements (see below) analogous to the proved rearrangement of aminophenylethyl carbonate. Recourse was had, therefore, in the final instance to methylation of oxyphenylurethane with diazomethane in neutral solution, following Von Pechmann's method for determining delicate questions of constitution. Von Pechmann² has shown that substances of an acid or a phenol character are easily methylated with this

¹ See preliminary report, *loc. cit.*, p. 1059.

² Ber. d. chem. Ges., 28, 855.

reagent in absolute ether solution, thus minimizing the probability of molecular rearrangements. Oxyphenylurethane gave with diazomethane, methoxyphenylurethane,



recognized by converting it into methoxyphenylurea,



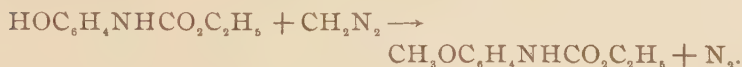
which was in every particular identical with a preparation made synthetically from *o*-anisidine or from *o*-anisidine-urethane. The constitution of *o*-oxyphenylurethane is consequently



and not

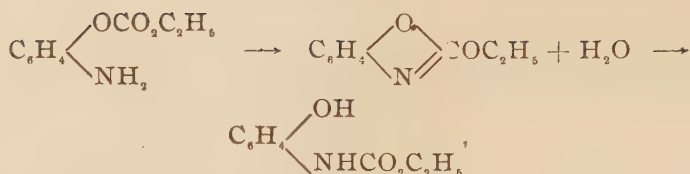


as decided in the preliminary report. The reaction with diazomethane is represented as follows :



The second object of this investigation, *viz.*, the study of the process of rearrangement of *o*-aminophenylethyl carbonate to oxyphenylurethane, was also carried out to a considerable degree. It was possible to isolate aminophenylethyl carbonate as the first product of the reduction of *o*-nitrophenylethyl carbonate in acid solution and as the first undoubted *o*-aminophenol ester known. Its hydrochloride is quite stable in dry condition; in aqueous solution it gradually goes over into oxyphenylurethane. But the free base, *o*-aminophenylethyl carbonate, is very much less stable—standing over night in a desiccator the oil is found to solidify to oxyphenylurethane—losing its basic properties and acquiring acid characteristics. This rearrangement of the free amine cannot possibly be due to the intermediate formation of the anhydro base, ethoxymethenylaminophenol, and its subsequent saponification, according to

¹ *Vide*, preliminary report, *Loc. cit.*



since the anhydro base is quite a stable body, having been preserved for months without excluding traces of moisture, and even in contact with water no such rapid change was observed as in the case of aminophenyl carbonate. This conclusion is confirmed by the fact that diacylaminophenols, $\text{Ac.NHC}_6\text{H}_4\text{OAc}'$, as shown below, apparently suffer similar rearrangement, even more readily than aminophenylethyl carbonate itself, and, in their case, an anhydro base as intermediate product is plainly impossible. Aminophenylethyl carbonate, therefore, suffers rearrangement without the intermediate formation of an anhydro base, as Böttcher was led to assume in the analogous case of the reduction of *o*-nitrophenyl benzoate. Nevertheless, an intermediate ring derivative is most likely formed for the following reasons:

1. *p*-Aminophenyl carbonate was found to be a perfectly stable compound, not liable to rearrangement—the rearrangement is peculiar to the ortho series.

2. The rearrangement occurs as long as the nitrogen atom holds at least one hydrogen atom, and no longer.

Thus the fact that the two reactions,



and



give one and the same substance, $\text{C}_6\text{H}_5\text{COOC}_6\text{H}_4\text{NHCO}_2\text{C}_2\text{H}_5$, (see below) is most likely due to similar rearrangements of the diacylaminophenols. But the analogous derivatives of methylaminophenol give two series of isomers; *e. g.*,

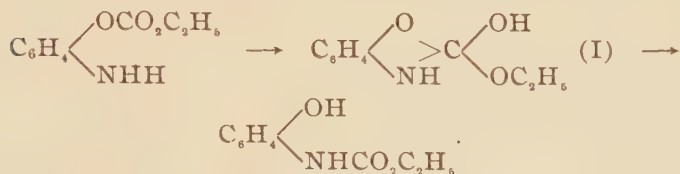


and



both of which have been prepared, which are perfectly stable substances. There is, therefore, no direct exchange of acyls in the kind of rearrangement under discussion: its de-

pendence on the hydrogen of the imide group points clearly to intermediate ring formations, which may be illustrated most simply in the rearrangement of aminophenylethyl carbonate itself:



It is obvious that at least one, but only one, reactive hydrogen atom of the amine group is essential to such rearrangements, and that the second one may be replaced by a second acyl group without interfering with the possibility of such ring transformations.

Thus, while oxyphenylurethane has not the ring constitution (I), there is every reason for believing that this ring compound has a transitory existence when aminophenylethyl carbonate goes over into oxyphenylurethane. No other rational explanation of the change seems possible on the basis of the experimental evidence presented. It follows then that derivatives, $\text{RC}(\text{OH})\text{NH}(\text{OR})$, of the ortho acids are formed, but have no stable existence even under the favorable conditions caused by a ring formation.

The unusual results obtained in preparing diacylamino-phenols, to which frequent reference has been made, require a few words of explanation. The same benzoyloxyphenylurethane (m. p. $75^\circ.5$, always giving by saponification with alkalis benzoic acid and oxyphenylurethane), was obtained by the following three reactions:

- a. The action of benzoyl chloride on oxyphenylurethane,



- b. The action of ethyl chlorformate on benzoylaminophenol in alkaline solution,



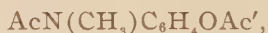
- c. The action of benzoyl chloride on aminophenylethyl carbonate in aqueous alkaline, or in ether, solution,



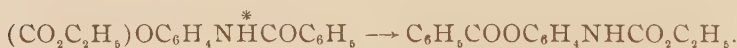
According to its behavior on saponification, and according to preparation *a* benzoyloxyphenylurethane seems to have the constitution $C_6H_5COOC_6H_4NHCOC_2H_5$ (A). According to preparations *b* and *c* and their behavior when heated (p. 6) benzoyloxyphenylurethane would be



Since the same body is produced only one of these formulæ can be the correct one. When an attempt is made to prepare the second compound it is evidently converted by rearrangement into the stable modification. Formula (A) probably represents the true constitution of the stable substance, for the reason that when saponified it yields benzoic acid and oxyphenylurethane. This method gave perfectly reliable results in determining the position of the acyl groups in the case of bodies of undoubted constitution in the methylaminophenol series,



where both series of isomers have been prepared and found to be stable. With these compounds, the acyl group attached to oxygen is, without exception, removed first by saponification with alkalis. When the compound (B) is formed by methods *b* and *c* it at once goes over into the form (A) as follows:



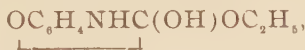
As the hydrogen atom $\overset{*}{H}$ is essential for the rearrangement (when it is replaced by methyl there is no rearrangement), intermediate ring derivatives must be formed first similar to that given on page 2 as representing the rearrangement of aminophenylethyl carbonate. It is even possible that in the case of the diacyl compounds such a ring derivative represents the final form of the stable modification; for example, benzoyloxyphenylurethane may be



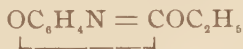
which would agree, in part, somewhat better with its behavior than the constitution (A) assigned to it.

It is noteworthy that it has been possible to isolate the two isomers, aminophenylethyl carbonate and *o*-oxyphenylurethane, and to observe the change of the former into the latter, but that contrary to expectation all endeavors to isolate the corresponding second isomeric benzoyl derivative (and the second nitrobenzoyl isomer) have thus far been unsuccessful. In fact the two isomers in the series of *o*-diacylaminophenols, $\text{AcOC}_6\text{H}_4\text{NHAc}'$ and $\text{Ac}'\text{OC}_6\text{H}_4\text{NHAc}$, have in no instance been obtained with absolute certainty as yet. In the case of Ac being made benzoyl ($\text{C}_6\text{H}_5\text{CO}$), and Ac' *m*-nitrobenzoyl ($\text{NO}_2\text{C}_6\text{H}_4\text{CO}$) substances were obtained, crystallizing persistently in different forms, but of practically the same melting-point, (152° and 153°) which was not depressed more than 4° (softening slightly at 146° , melting at 149° – 153°) on mixing the two substances. The one crystal form was twice observed to change over into the other and remain so permanently,¹ and both compounds gave the same saponification products. It is somewhat uncertain, therefore, whether they really represent chemical isomers of the two series just mentioned, but it is probable that they do. Further investigation of the constitution of the stable compounds obtained will be carried out, and further attempts made to isolate isomers in this series and observe the conditions of their change to the stable forms.

The work involved in attaining the first two objects of this investigation—determining the constitution of oxyphenylurethane and studying the rearrangements in this group—left but little time for taking up the third object, a study of the connection between the ring derivative,



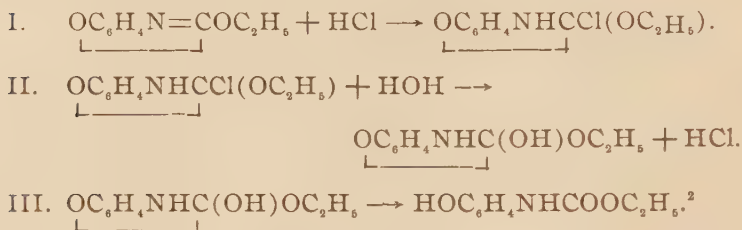
and the hydrochloride of ethoxymethenylaminophenol,



(see p. 2). As the ring derivative has only a transitory existence in the rearrangement of *o*-aminophenylethyl carbonate to *o*-oxyphenylurethane (p. 11) the basis for an experimental investigation seemed too slight for much work in this direc-

¹ *Vide*, experimental part.

tion at present. It was shown that the above hydrochloride gives, by hydrolysis, oxyphenylurethane under the same conditions that aminophenylethyl carbonate does. The reactions are exactly in accord with what was to be expected from hydrolysis¹ of the hydrochloride of an imido ether formed by the addition of hydrochloric acid to the double bond of ethoxymethenylaminophenol:²



A more thorough investigation, for instance, of the reversibility of reaction II is necessary, to make the reactions of permanent value for the theory of the constitution of imidoether salts.

EXPERIMENTAL PART.

Reduction of o-Nitrophenylethyl Carbonate.

Oxyphenylurethane, $\text{HOC}_6\text{H}_4\text{NHCOOC}_2\text{H}_5$.—The reduction was carried out at first in alcoholic solution, according to Bender's directions: 27 grams of *o*-nitrophenyl carbonate were dissolved in alcohol, 65 cc. of concentrated hydrochloric acid added, and then slowly 40 grams of powdered tin. The whole was kept cool with ice-water. After three hours the solution was filtered and about an equal quantity of water added. Immediately an oil separated which slowly crystallized on being placed in ice-water. The melting-point of the crystals was 72° – 83° . After crystallizing the substance three times from water and then precipitating it from a solution in benzene with ligroin, the melting-point remained constant at 86° . On heating the filtrate, from the oil which first separated, and then allowing it to cool slowly, more crystals sepa-

¹ Stieglitz: This JOURNAL, 21, 106.

² Stieglitz: *Ibid.*, *Loc. cit.*

rated which had the melting-point 85° . If, however, the filtrate was allowed to stand without heating, crystals began to separate only after some hours, and then continued to form for some days. The melting-point was the same in both cases.

A quicker method of carrying out the reduction is to use a concentrated aqueous acid solution: 25 grams of the nitro carbonate are put in a flask with 60 cc. of concentrated hydrochloric acid and very little water, then 40 grams of tin slowly added, and the whole kept cold in ice-water during the first part of the action, it being allowed finally to reach the ordinary temperature. When the solution has become clear (in about forty-five minutes) it is filtered through glass-wool, after the addition of about an equal volume of water, and heated nearly to boiling for a few minutes. An oil separates which, on cooling, becomes a solid mass of crystals. On recrystallizing twice from water the melting-point is $86^{\circ}.5$. If the solution, during reduction, is allowed to become quite warm, mixtures result which melt between 70° and 130° , consisting of oxyphenylurethane (m. p. 86°) and carbonylaminophenol (m. p. 137°). This was proved by separating the mixture, by fractional precipitation, from a solution in benzene by carefully adding ligroin. Incidentally the presence of carbonylaminophenol was shown on treating a sample of oxyphenylurethane, which happened to contain some carbonylaminophenol, with diazomethane. Crystals separated in this case from the methoxyphenylurethane, which is an oil, and these were identified as carbonylmethylaminophenol (m. p. 86°), by comparison with the synthetic compound.

The oxyphenylurethane, prepared as described, crystallizes in rather short, thick needles or plates, varying somewhat with the medium from which it is crystallized. It is soluble in most of the organic solvents except ligroin, somewhat soluble in cold water, much more so in boiling water. It is soluble in cold, dilute, caustic alkalis, from which solution it is precipitated unchanged by acids. The crude crystals (m. p. 72° – 83°) deposited from the acid solution invariably dissolved completely in dilute alkali. The change into oxyphenylurethane was, therefore, not effected by the process of purification

but occurred in the original acid solution. From a concentrated solution in the alkalis the potassium and sodium salts crystallize in large needles.

Analyses of oxyphenylurethane, obtained by reduction of *o*-nitrophenylethyl carbonate, gave the following results :

I. 0.2485 gram substance gave 0.5410 gram CO_2 , and 0.1371 gram H_2O .

II. 0.3244 gram substance gave 21.5 cc. N at 15.75° and 749.1 mm (corr.).¹

	Calculated for $\text{C}_9\text{H}_{11}\text{NO}_3$.	Found.
C	59.66	59.35
H	6.07	6.12
N	7.73	7.76

For comparison with Bender's product, oxyphenylurethane was also prepared according to Groenvik's² method, by treating *o*-aminophenol (2 mols.) in ethereal solution with ethyl chlorformate (1 mol.). Transparent, thick needles separated out on partial evaporation, and these were recrystallized from hot water. The melting-point was then 86.5° , and in appearance the compound was similar to the substance obtained by reduction of nitrophenylethyl carbonate. Mixtures of the two had the same melting-point as either separately.

Benzoyloxyphenylurethane, $\text{C}_6\text{H}_5\text{COOC}_6\text{H}_4\text{NHCO}_2\text{C}_2\text{H}_5$.—In order more fully to establish the identity of the two substances as oxyphenylurethane, the benzoate was obtained from both preparations. Each of the substances was dissolved in a solution of potassium hydroxide (1 mol.). In each case an oil separated which, when shaken, hardened to a crystalline mass. This was recrystallized twice from alcohol, to which a little water had been added. The melting-point of each, as well as that of a mixture of the two, was 75.5° . Both were insoluble in alkalis and acids, very soluble in warm alcohol and most of the organic solvents. About 90 per cent of the theoretical yield was obtained.

I. 0.1696 gram substance gave 7.9 cc. N at 19.2°C . and 744.7 mm. (corr.).

¹ Corrected for vapor-tension over 30 per cent caustic potash.

² Bull. Soc. Chim., **25**, 177.

II. 0.3305 gram substance gave 15 cc. N at 23°.5 C. and 735.3 mm (corr.).

	Calculated for $C_{16}H_{16}NO_4$.	I.	Found.	II.
N	4.91	5.35		5.08

Benzoyloxyphenylurethane was also obtained by treating benzoyl-*o*-aminophenol with ethyl chlorformate.

Benzoyl-o-aminophenol, $C_6H_5CONHC_6H_4OH$. — This substance was first made by Hübner,¹ but the following method was found to give satisfactory results: 1 gram (2 mols.) of *o*-aminophenol was suspended in absolute ether, and 0.5 gram (1 mol.) of benzoyl chloride then slowly added to the mixture. A reaction began at once, the hydrochloride of 1 molecule of the base being precipitated, mixed with some of the benzoyl derivative which is not very soluble in ether. The hydrochloride was dissolved out with water, the ether solution washed with dilute hydrochloric acid and water, and the ether then evaporated. The benzoylaminophenol so prepared melted at 165°–167° (with decomposition), was soluble in alkalis, and had all the properties of Hübner's product.

Action of Ethyl Chlorformate on Benzoyl-o-aminophenol.

Three grams of benzoyl-*o*-aminophenol were dissolved in a little more than 1 molecule of potassium hydroxide and 1.5 grams (1 mol.) of ethyl chlorformate added. An oil separated out which solidified when shaken. The substance is very soluble in alcohol and ether, fairly soluble in ligroin (40°–60°), from which it crystallizes in white needles. After three recrystallizations the melting-point was constant at 76°.5.

0.2380 gram substance gave 0.5848 gram CO_2 , and 0.1143 gram H_2O .

	Calculated for $C_{16}H_{16}NO_4$.	Found.
C	67.36	67.01
H	5.26	5.33

As the melting-point was so near that of its supposed isomer, obtained from oxyphenylurethane and benzoyl chloride in alkaline solution, and as the appearance of the two was so similar, more of that isomer was made and carefully purified

¹ Ann. Chem. (Liebig), 210, 387.

by recrystallizing it from ligroin. The melting-point now became $76^{\circ}.5$, and that of a mixture of the two was the same. Neither substance decomposed at the melting-point, which was unchanged after the substance solidified on cooling. The substances obtained from benzoyl chloride and oxyphenylurethane on the one hand, and from benzoylaminophenol and ethyl chlorformate on the other hand, are therefore identical. This unexpected conclusion was confirmed by a study of the saponification products of the two substances.

One gram of benzoyloxyphenylurethane (prepared from benzoylaminophenol) was shaken for an hour with a dilute aqueous solution of caustic potash (2 mols.), warming slightly toward the end. Nearly all went into solution. After acidifying, the mixture was extracted with ether, the ethereal solution shaken out with bicarbonate of soda, dried, and the ether evaporated. After recrystallizing from hot water the residue melted at 83° ; mixed with *o*-oxyphenylurethane the melting-point was 84° , and it showed all the properties of this substance. The bicarbonate solution was acidified and extracted with ether, a substance being thus obtained whose odor and melting-point characterized it as benzoic acid.

Some of the benzoyloxyphenylurethane (p. 16) prepared from oxyphenylurethane and benzoyl chloride was saponified exactly as described above, and gave the same products—benzoic acid and oxyphenylurethane, thus confirming the identity of the two substances. Consequently some rearrangement in the molecule of one (or both) of them must have occurred. According to the saponification-products the stable substance is benzoyloxyphenylurethane,



The attempt to prepare the two possible isomers was repeated, the solutions being kept below 5° , in the hope that, at this temperature, real isomers might be isolated. The substances, however, were identical in every way with those described above, as proved both by appearance and melting-point as well as by saponification in alcoholic potash, which could be accomplished in one or two minutes. As seen under a microscope, no difference could be distinguished between the crys-

tal forms. Both appeared as small, well-formed prisms with end faces perpendicular to the long axis. Finally, the two substances were prepared at -5° , at once washed with water, acid, and alcohol, and then immediately saponified by means of alcoholic potash. The same saponification-products were obtained, showing that one of the isomers did not change into the other stable modification in purifying it, but in preparing it.

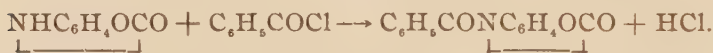
Dry Distillation of Benzoyloxyphenylurethane.

Several grams of the dry substance were heated in an Anschütz distilling flask until the thermometer in the vapor had reached 100°C . The liquid collected in the receiver was then poured off and shown to be alcohol by the iodoform test. The flask was then heated again under somewhat reduced pressure, until crystals began to appear in the neck of the receiver. The liquid in the receiver was again poured off and, by its odor and boiling-point (213°), proved to be benzoic ether. A vacuum was again secured and most of the residue distilled at 200° – 220° . A solid distillate collected in the receiver. This was digested some time with caustic soda, and filtered. The filtrate was acidified and extracted with ether. On evaporating the ether a small amount of a very impure substance was obtained, melting at 85° – 105° . It was probably impure carbonylaminophenol, but was not further investigated. The larger part of the solid distillate was insoluble in alkali and was washed with acidified water, then with pure water, and finally recrystallized once from alcohol, in which it is soluble with difficulty. Crystals were obtained melting at 174° and possessing all the properties of benzoylcarbonylaminophenol, which will be described presently. When water was added to the mother-liquor from the first crystallization from alcohol, crystals were deposited which were very soluble in alcohol and melted at 97° – 101° . Some of the substance, sublimed *in vacuo*, melted at 102° . The crystals were long needles soluble in cold ether and benzene, less soluble in ligroin, somewhat soluble in boiling water, slightly in dilute sulphuric acid, quite soluble also in concentrated hydrochloric acid, reprecipitated by alkalies. It was suspected that this

substance was benzenylaminophenol (m. p. 101° – 103°), and this was confirmed by preparing the latter synthetically according to the method described by Ladenburg.¹ The melting-point and properties of the substance were the same as those described above, and a mixture of the two had the same melting-point.

Benzoylcarbonyl-o-aminophenol, $\text{C}_6\text{H}_5\text{CONC}_6\text{H}_4\text{OCO}$. — By

distilling oxyphenylurethane, alcohol is given off and carbonylaminophenol is formed. As in distilling benzoyloxyphenylurethane alcohol was formed in large quantities, it was concluded that the substance melting at 174° was the corresponding benzoylcarbonylaminophenol. This substance is not described in the literature, so that it became necessary to prepare it synthetically. This was done by treating carbonylaminophenol in alkaline solution with benzoyl chloride :

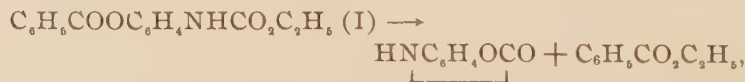


Recrystallized from alcohol the substance melts at 174° .

0.2851 gram substance gave 14.8 cc. of nitrogen at 18° , and 730.3 mm. (corr.).

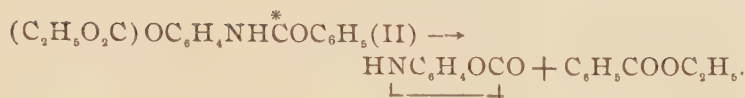
	Calculated for $\text{C}_{14}\text{H}_9\text{NO}_3$.	Found.
N	5.85	5.88

By mixing equal portions of this substance with that formed by distillation (m. p. 174°) the melting-point was not lowered. The two are identical. The products of the dry distillation of benzoyloxyphenylurethane are therefore chiefly alcohol and benzoylcarbonylaminophenol, to a small extent ethyl benzoate and carbonylaminophenol, and finally some benzenylaminophenol. The formation of ethyl benzoate and carbonylaminophenol according to

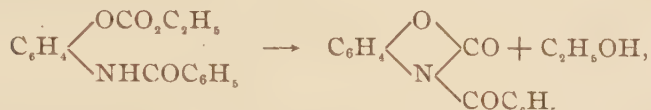


is perhaps in better accord with the constitution assigned to benzoyloxyphenylurethane than with the other possible open-chain form,

¹ Ber. d. chem. Ges., 9, 1526.



The formation of these compounds would involve the separation of carbon atom $\overset{*}{\text{C}}$ from nitrogen, which does not occur as easily as from oxygen. But it is particularly worthy of note that the main products of the dry distillation of benzoyloxyphenylurethane are decidedly in better accord with this isomeric form¹ than with the one chosen on the basis of the saponification-products.

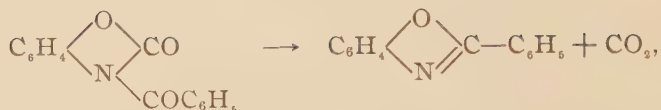


appears as a very simple and likely reaction, but the formation of the same products from



evidently would involve a much more complicated reaction since the benzoyl group is finally found attached to nitrogen. Much value was attached to this fact in my preliminary report—rightly it seems as long as molecular rearrangements of the diacyl compounds were not to be considered. But since these must take place under much simpler conditions below 0° , their occurrence in the process of dry distillation would not now be surprising. More work, however, has been planned for the study of these conditions. It may be mentioned, in this connection, that the dry distillation of the otherwise analogous *m*-nitrobenzoyloxyphenylurethane does not yield any *m*-nitrobenzoylcarbonylaminophenol. In this case the chief product is *m*-nitrobenzenylaminophenol, corresponding to the decomposition-product obtained from benzoyloxyphenylurethane in smallest quantity—the anhydro base, benzenylaminophenol. The formation of this substance acquires special interest therefrom. It was suspected that it is formed from benzoylcarbonylaminophenol as follows :

¹ Or with the ring form, see preliminary report, *loc. cit.*, p. 1063, and introduction, p. 6.



and it was shown that pure benzoylcarbonylaminophenol, when distilled, does decompose to some extent in the manner indicated. This may account for the fact that, in the case of *m*-nitrobenzoyloxyphenylurethane, as the *m*-nitrobenzoylcarbonylaminophenol disappears from the distilled product, the amount of anhydro base is proportionately increased. But it has also awakened the suspicion that the first action of heat may be to form alcohol and benzoyloxyphenyl isocyanate:¹



This could very well be converted into benzoylcarbonylaminophenol, or lose carbon dioxide, and give benzenylaminophenol. The preparation of this isocyanate will, therefore, be one of the first steps in the further study of these derivatives.

The result of the one case already given, in which the same substance is formed in whatever order the two acyl groups are introduced into the *o*-aminophenol molecule, was so unexpected that its correctness was tested by the use of other acyl radicals, in order to determine whether it holds, in general, for diacyl-*o*-aminophenols. *m*-Nitrobenzoyl chloride being easily available, it was first used in place of benzoyl chloride.

m-Nitrobenzoyloxyphenylurethane,

$\text{NO}_2\text{C}_6\text{H}_4\text{COOC}_6\text{H}_4\text{NHCO}_2\text{C}_2\text{H}_5$, was prepared from oxyphenylurethane and *m*-nitrobenzoyl chloride in alkaline solution. Recrystallized from alcohol it melts at 86°.5.

I. 0.2425 gram substance gave 0.5147 gram CO_2 , and 0.1032 gram H_2O .

II. 0.2541 gram substance gave 0.5388 gram CO_2 , and 0.0992 gram H_2O .

III. 0.2698 gram substance gave 16.9 cc. N at 18°, and 730.4 mm. (corr.).

IV. 0.2523 gram substance gave 17.3 cc. N at 19°, and 734.9 mm. (corr.).

V. 0.2085 gram substance gave 16.2 cc. N at 20°, and 728.8 mm. (corr.).

¹ Vide Hofmann: Ber. d. chem. Ges., 14, 2727; Folin: This JOURNAL, 19, 338.

	Calculated for $C_{16}H_{14}N_2O_6$.	I.	II.	Found. III.	IV.	V.
C	58.18	57.88	57.81			
H	4.24	4.70	4.32			
N	8.48			7.09	7.78	8.72

In the first two estimations of nitrogen, nitrite was found in the potash solution. Therefore the last analysis was made in a long furnace with the introduction of a spiral of reduced copper 12 to 15 inches in length.

The substance is soluble in alcohol, ether, and benzene, almost insoluble in ligroin, and insoluble in alkalis and acids. By dissolving in benzene and then adding ligroin, very fine prisms are formed.

Three grams of the substance (m. p. $86^\circ.5$) were saponified in the cold by alcoholic potash (2 mols.) and the products isolated in the usual manner. They were found to be oxyphenylurethane and *m*-nitrobenzoic acid, having all the properties of the synthetic products. A very small amount of ethyl *m*-nitrobenzoate (m. p. 40° – 42°) was also recovered. The only products of the saponification of *m*-nitrobenzoyloxyphenylurethane are, therefore, *m*-nitrobenzoic acid and oxyphenylurethane. To a slight extent ethyl *m*-nitrobenzoate is split from the molecule, exactly as occurs on heating the substance. No *m*-nitrobenzoylaminophenol is formed.

Five grams of *m*-nitrobenzoyloxyphenylurethane (m. p. $86^\circ.5$) were heated in a metal bath to 250° – 260° , an Anschütz flask being used. Alcohol was driven off, and also a small amount of a solid melting at 80° – 123° . The flask was then exhausted and the contents distilled. Some decomposition occurred, giving a slight odor of aniline. About 2.5–2.75 grams of distillate were obtained. This was ground in a mortar with alkali, and filtered. On acidifying the filtrate a small amount of a white solid separated, which proved to be a mixture of *m*-nitrobenzoic acid and carbonylaminophenol. The neutral residue (chief part) was then boiled out with very little alcohol, to remove *m*-nitrobenzoic ether. On adding water to the filtrate a solid separated, which melted at 38° – 41° , and proved to be this ether. The greater part was found to be almost insoluble in alcohol, ether, and acetone ;

fairly soluble in chloroform and acetic acid, depositing a white solid melting at 203° – 205° . Recrystallized from a large amount of absolute alcohol, the melting-point was raised to 207° , resolidifying at 200° . The compound is also soluble in concentrated hydrochloric acid, but is reprecipitated on adding water. Reasoning from the results of the work on the benzoyl derivative, it was thought to be either *m*-nitrobenzoylaminophenol or *m*-nitrobenzenylaminophenol, and was shown to be the latter by comparing it with synthetic preparations of these substances.

m-Nitrobenzoylcarbonylaminophenol,
 $\text{NO}_2\text{C}_6\text{H}_4\text{CO}-\text{NC}_6\text{H}_4\text{OCO}-\text{L}-\text{L}-\text{L}$

aminophenol and *m*-nitrobenzoyl chloride in caustic soda solution gave this substance. On recrystallizing from alcohol, in which it is very difficultly soluble, it becomes pure white and melts at 199.5 – 201.5 , but resolidifies at 180° , again melting at the same temperature as before. Mixed with the substance of melting-point 207° , obtained in the dry distillation of *m*-nitrobenzoyloxyphenylurethane, the melting-point was depressed to 175° – 193° , showing that the substances are not identical. It is practically insoluble in ether, ligroin, alkalies, and concentrated hydrochloric acid, somewhat soluble in acetic acid, easily in chloroform. The purity of the substance was controlled by an analysis:

0.1986 gram substance gave 0.4289 gram CO_2 , and 0.0545 gram H_2O .

	Calculated for $\text{C}_{14}\text{H}_8\text{N}_2\text{O}_6$.	Found.
C	59.15	58.89
H	2.81	3.04

m-Nitrobenzenyl-*o*-aminophenol, $\text{C}_6\text{H}_4(\text{NO}_2)\text{C}=\text{NC}_6\text{H}_4\text{O}-\text{L}-\text{L}-\text{L}$

This anhydro base was prepared by heating molecular quantities of *o*-aminophenol and *m*-nitrobenzoyl chloride. The residue was difficultly soluble in alcohol, but recrystallized from this solvent in light grayish-yellow crystals of melting-point 207° , resolidifying at 200° . Mixed with the substance having the same melting-point, obtained by distilling *m*-nitrobenzoyloxyphenylurethane, no depression was observed. The

two substances are therefore identical. Mixed with *m*-nitrobenzoylcarbonylaminophenol (m. p. 199° – 201°) the melting-point was depressed 25° . The anhydro base is difficultly soluble in most organic solvents, except chloroform, but is soluble in concentrated hydrochloric acid, and is reprecipitated by adding water.

0.1052 gram substance gave 0.2498 gram CO_2 , and 0.0346 gram H_2O .

	Calculated for $\text{C}_{13}\text{H}_8\text{N}_2\text{O}_3$.	Found.
C	65.00	64.76
H	3.33	3.61

The high-melting product of the dry distillation of nitrobenzoyloxyphenylurethane is, consequently, *m*-nitrobenzenyl-*o*-aminophenol. It is evident, therefore, that in distilling the molecule lost both alcohol and carbon dioxide. Several attempts were made to split off the first alone, by heating to different temperatures, but without success—both coming off at the same temperature, as was proved. The amount of the high-melting substance was always much less than the theoretical. On that account a roughly quantitative experiment was carried out as follows: 4.75 grams were slowly heated in a metal bath to 125° . The loss in weight, 0.2 gram, was apparently a little moisture. Pure, dry air was drawn through the flask into lime-water, but no trace of carbon dioxide was found; nor had the melting-point of the substance changed. Heating was continued until the first indication of decomposition, 195° , and the temperature kept between this and 200° as long as action was visible. A very little oil had distilled, and the presence of alcohol and carbon dioxide was proved. The residue now weighed 4 grams. This was digested with cold alcohol and filtered into a tared beaker. When the alcohol had evaporated the residue weighed 2.63 grams. After boiling out the more insoluble part with a very little alcohol it weighed 0.8 gram, so that a large part was soluble in cold alcohol. The part soluble in cold alcohol was digested with caustic soda and filtered. On acidifying the filtrate a solid was deposited, which, after recrystallization from alcohol and water, was not quite pure, melting at 133° – 135° , and proved

to be carbonylaminophenol by the usual tests. The oily residue, insoluble in alkali, solidified on standing, melted at 38° – 40° , and gave all the tests for *m*-nitrobenzoic ether. The most insoluble part, as well as that soluble in boiling alcohol, were mixtures melting from 150° – 180° . No simple substance could be separated by recrystallization, but on heating them to 250° they were converted into *m*-nitrobenzenyl-*o*-aminophenol (m. p. 207°). It is evident that in the dry distillation of *m*-nitrobenzoyloxyphenylurethane the decomposition into ethyl nitrobenzoate and carbonylaminophenol occurs to a larger degree than in the case of benzoyloxyphenylurethane (page 8). The decomposition reactions, into nitrobenzoylcarbonylaminophenol, and of this into nitrobenzenylaminophenol, seem to occur at the same temperature, so that the anhydro base becomes one of the main products. The theoretical bearing of this has already been discussed (page 10).

As the substance by heat could not be made to lose alcohol alone, a little was dissolved in concentrated sulphuric acid and allowed to stand about five minutes. Then water was added slowly, when a solid separated which was recrystallized from much hot alcohol. The melting-point was 199° – 201° , and mixed with *m*-nitrobenzoylcarbonylaminophenol, made synthetically and melting at this point, no depression of the melting-point was observed. We have here again the peculiar fact that the *m*-nitrobenzoyl group is found attached to nitrogen, while the above synthesis and saponification of *m*-nitrobenzoylurethane show it attached to oxygen, unless, indeed the diacyl-*o*-aminophenols have a ring constitution, which the monoacyl derivatives have been proved not to possess (page 9, introduction).

m-Nitrobenzoyl-*o*-aminophenol, (*m*)- $\text{O}_2\text{NC}_6\text{H}_4\text{CONHC}_6\text{H}_4\text{OH}$.—To 2 grams (2 mols.) of *o*-aminophenol, suspended in ether, an ether solution of 1.7 grams (1 mol.) of *m*-nitrobenzoyl chloride was added. The ethereal filtrate gave a small yield of a substance melting at 207° . The solid which was precipitated in the ether solution was washed with water to remove the hydrochloride of aminophenol. Recrystallized from alcohol, the substance was obtained in short, thick prisms of a light-yellow color, melting at 207° . Nitrobenzoylaminophe-

nol dissolves in alkalis, forming a bright-yellow solution, and is reprecipitated unchanged on addition of dilute acids.

Action of Ethyl Chlorformate on m-Nitrobenzoyl-o-aminophenol.—3.35 grams of the nitrobenzoylaminophenol were dissolved in a little more than the calculated amount (1 mol.) of potassium hydroxide in solution, and 1.5 grams (1 mol.) of ethylchlorformate added. On shaking a solid separated in a somewhat oily condition. It was extracted with ether, but this solution immediately commenced to deposit crystals. The substance was purified by dissolving in benzene and carefully adding ligroin. The melting-point was found to be $86^{\circ}.5$. The yield was quantitative.

0.1335 gram substance gave 0.2845 gram CO_2 , and 0.0536 gram H_2O .

	Calculated for $\text{C}_{16}\text{H}_{14}\text{N}_2\text{O}_6$.	Found.
C	58.18	58.12
H	4.24	4.42

The substance has the same appearance, crystalline form, and melting-point as its supposed isomer, *m*-nitrobenzoyloxyphenylurethane, and the melting-point of a mixture of the two is the same as that of either, proving the identity of the compounds. This was fully confirmed by the result of saponifying the substance whose preparation has just been described.

Two and three-tenths grams of the substance treated with alcoholic potash, as described for *m*-nitrobenzoyloxyphenylurethane, gave 0.93 gram *m*-nitrobenzoic acid (m. p. 139° – 141°) and 1.18 grams oxyphenylurethane, which softened at 79° but melted at 84° . The melting-point was raised a little by mixing with pure oxyphenylurethane. These are the same saponification-products as *m*-nitrobenzoyloxyphenylurethane gives. Again the action of ethyl chlorformate on nitrobenzoyl-*o*-aminophenol,



and of nitrobenzoyl chloride on oxyphenylurethane,



give the same substance which, according to the saponification-products, is *m*-nitrobenzoyloxyphenylurethane,



A molecular rearrangement must then convert the isomer into this same compound.

Diacyl-*o*-aminophenols were also prepared, benzoyl and nitrobenzoyl being used as the two acyl radicals, without any carbethoxy group, particularly in order to determine whether their abnormal behavior—originally in excellent agreement with a ring formation, now considered to be due to rearrangements by means of ring formations—is dependent in any way on the reactivity of the carbethoxy group. The preliminary work indicated a difference of 15° in the melting-points of the two substances, benzoylaminophenol *m*-nitrobenzoate and *m*-nitrobenzoylaminophenol benzoate. By further purification, however, this difference was reduced to hardly 1° . The saponification-products of both substances were repeatedly found to be identical. However, the general appearance and crystalline forms remained persistently so different that I was led to a careful and exact reinvestigation of the reaction under different conditions. The results were the same, so that I shall describe only those conditions which seem to me to be the most favorable for the production and identification of isomeric bodies.

m-Nitrobenzoyl-*o*-aminophenol Benzoate,

$\text{NO}_2\text{C}_6\text{H}_4\text{CONHC}_6\text{H}_4\text{OCOC}_6\text{H}_5$.—1.29 grams of *m*-nitrobenzoyl-*o*-aminophenol, freshly made and carefully purified, were dissolved in a solution of sodium hydroxide (1 mol.) at 0° , and 0.7 gram (1 mol.) of cold benzoyl chloride added, the whole being well shaken. The separated solid was filtered, washed with alkali, then thoroughly with water. A little was dried, and without being crystallized it melted at 148° – 151° . The rest was washed with cold alcohol; a little dissolved which had the melting-point 151° – 153° . Some was recrystallized twice from alcohol; it then melted at 153° .

0.2486 gram substance gave 17.4 cc. N at 22° C., and 726.9 mm. (corr.).

	Calculated for $\text{C}_{20}\text{H}_{14}\text{N}_2\text{O}_6$.	Found.
N	7.73	7.78

The crystals were long, white, hair-like needles, not very soluble in alcohol, insoluble in alkalies and acids. 3 grams

of the substance, without crystallization, were treated with alcoholic potash in excess. In one minute all had dissolved, and this was not precipitated on adding water. The solution was acidified immediately, extracted with ether, the extracts washed with water, and a solution of sodium bicarbonate (*B*), dried with calcium chloride, and the ether evaporated. This residue (*A*) containing the monoacylaminophenols was dissolved in alkali and extracted with ether to remove any of the original substance, and again acidified. A solid separated which was recrystallized several times. The melting-point was about 160° , though not sharp. A little was dissolved in alkali and benzoyl chloride added. A solid formed, melting at 178° , 2° above that given for dibenzoyl-*o*-aminophenol. To remove any trace of *m*-nitrobenzoyl-*o*-aminophenol, the monoacylaminophenol was dissolved in alcohol, ammonia added, and hydrogen sulphide passed through the solution to reduce the nitro body. After evaporation the solid residue was washed with acid and water, then recrystallized from alcohol. It now softened at 164° , melting at 165° – 167° . Mixed with benzoyl-*o*-aminophenol this was not depressed, showing that (*A*) consisted chiefly of this substance. The carbonate solution (*B*) was acidified and extracted with ether, yielding a substance melting at 139° – 141° , and with all the properties of *m*-nitrobenzoic acid. The benzoate of *m*-nitrobenzoylaminophenol gives, therefore, as the chief products of saponification *m*-nitrobenzoic acid and benzoylaminophenol, in which the benzoyl group is attached to nitrogen, in the position originally held by the other acyl radical. Only traces of benzoic acid and *m*-nitrobenzoylaminophenol are formed. The substance was saponified also in warm hydrochloric acid, a little alcohol being used as solvent. The products were the same as those in alkaline solution.

Benzoyl-o-aminophenol-m-nitrobenzoate,

$\text{C}_6\text{H}_5\text{CONHC}_6\text{H}_4\text{OCOC}_6\text{H}_4\text{NO}_2$.—4 grams of benzoyl-*o*-aminophenol were dissolved in caustic soda, 3.5 grams (1 mol.) of *m*-nitrobenzoyl chloride (in ether) added, and the whole shaken for some time. The separated solid was washed and then recrystallized from alcohol. After the first recrystallization the melting-point was constant at 152° . The crystals be-

ing colored, they were boiled with alcohol and bone-black, filtered, then allowed to crystallize. If heated very slowly the substance now melted at 151° . It was dried at 100° and analyzed.

0.1178 gram substance gave 0.2862 gram CO_2 , and 0.0433 gram H_2O .

	Calculated for $\text{C}_{20}\text{H}_{14}\text{N}_2\text{O}_6$.	Found.
C	66.29	66.21
H	3.86	4.07

The substance crystallizes persistently in short, thick prisms, quite unlike the hair-like needles described above.

Two grams of the substance were shaken with a solution containing 2 molecules of caustic potash, heat being applied toward the end. Nearly all went into solution. After filtering and acidifying, the solution was extracted with ether, the ether solution washed with a solution of sodium bicarbonate (*B*), and the ether allowed to evaporate. The residue (*A*) containing monoacylaminophenol was boiled with water, then dissolved in alcohol, boiled with bone-black, and filtered. The crystals were then digested with a very little cold ether. Nearly all dissolved, leaving but a small amount of a substance melting at 204° – 207° , which was recognized as *m*-nitrobenzoyl-*o*-aminophenol by the fact that a mixture of the two had the same melting-point. The chief part of (*A*), soluble in ether, on further purification softened at 158° and melted at 163° . It is evidently benzoyl-*o*-aminophenol mixed with a trace of the nitro body, but this was not removed as in the former case. The bicarbonate solution (*B*) when acidified and extracted with ether, left a substance melting at 136° – 138° and having somewhat the odor of benzoic acid. It has all the properties of *m*-nitrobenzoic acid (m. p. 141°). The chief saponification-products of the *m*-nitrobenzoate of benzoylaminophenol are therefore *m*-nitrobenzoic acid and benzoylaminophenol, the same as those of the benzoate of *m*-nitrobenzoyl-*o*-aminophenol. But, exactly as in the case of the latter, very small quantities of benzoic acid and nitrobenzoylaminophenol are also formed—the latter containing the nitrobenzoyl group attached to nitrogen where the benzoyl group was originally held.

The melting-point of a mixture of benzoyl-*o*-aminophenol-*m*-nitrobenzoate,

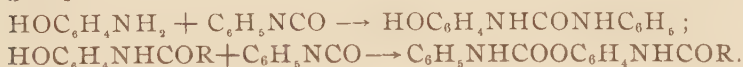


(m. p. 152°), and *m*-nitrobenzoyl-*o*-aminophenol benzoate,



(m. p. 153°), was less exact than that of either separately, as it softened slightly at 146° and melted at 149°–153°. The saponification-products are the same but the crystal forms are persistently different. The solubility of the two forms, in alcohol, are 31.16 per cent and 27.5 per cent, respectively. Many attempts were made to change one form of crystals into the other, but under no conditions could more than a trace of the hair-like needles be changed into the prisms, and never any in the opposite direction. The closeness of the melting-points, the identity of the saponification-products,¹ and the fact that by mixing the two substances the depression of the melting-point is very slight, while, as a rule, in this series, such a mixture causes a depression of 15°–20°, raise some doubt as to the isomerism of the two substances. The persistent difference in crystal form and the like difference in solubility, make it very probable, on the other hand, that they are isomers. In that event, however, rearrangement must occur either just before or just after saponification, unless the substances are indeed ring derivatives.

One other attempt was made to obtain more sharply defined isomers of the two diacyl-*o*-aminophenol series by means of phenyl isocyanate. Leuckart has shown² that phenyl isocyanate, in the presence of aluminium chloride, unites with the amide group in *o*-amidophenol, but that in substituted *o*-amidophenols the isocyanate reacts with the hydroxyl group :



Carbethoxyaminophenol Phenylcarbamate,



¹ See p. 38 as to the saponification-products of the two corresponding undoubtedly isomeric diacyl derivatives of methylaminophenol.

² J. prakt. Chem., 41, 301.

Five grams of oxyphenylurethane and a little more than 1 molecule of phenyl isocyanate were mixed in solution in absolute ether, and a small amount of aluminium chloride slowly added. The solution became warm and the odor of hydrogen chloride was noticed. After standing some hours, and being shaken at intervals, an oil settled out. On evaporating the ether, and washing with water and hydrochloric acid, the oil solidified. On dissolving in alcohol a small amount of carb-anilide was separated. After recrystallizing several times the melting-point was constant at 116° – 118° .

0.1215 gram substance gave 10.5 cc. N at 20° .5 C. and 726.6 mm. (corr.).

	Calculated for $C_{16}H_{16}N_2O_4$.	Found.
N	9.33	9.65

The substance crystallizes in small, nearly white, prisms and is fairly soluble in most of the usual solvents, but is insoluble in alkalies and acids.

Action of Ethyl Chlorformate on Oxydiphenylurea.

Chemically pure oxydiphenylurea¹ (m. p. 167°) prepared according to Leuckart, was dissolved in sodium hydroxide, and ethyl chlorformate (1 mol.) added. An oil separated which was extracted with ether. The ether solution was washed with alkali, water, acid, then again with water until it gave no test for acid. The solution was dried for from fifteen to eighteen hours with fused sodium sulphate and the ether evaporated. It was then put in a vacuum over sulphuric acid for three days. It did not crystallize, nor would it crystallize on being cooled for a day to -10° – -30° (cold winter night). It is insoluble in acid and alkalies, easily soluble in most of the organic solvents. As the oil could not be purified by distillation it was analyzed.

0.2867 gram substance gave 18.9 cc. N at 21° C. and 729 mm. (corr.).

	Calculated for $C_{16}H_{14}N_2O_4$.	Found.
N	9.33	7.37

The oil was apparently quite impure, but it is evidently not

¹ Leuckart gives the melting-point at 163° – 165° .

identical with the substance just described (m. p. 116°-118°), as it could not be made to crystallize by inoculation with a crystal of that substance. The small amount of the oil that remained was saponified, after standing a couple of months, with the result that, instead oxydiphenylurea, a few crystals of oxyphenylurethane were obtained. This result is as difficult to explain, on the assumption of an unchanged open chain, as those obtained with the other acyl derivatives, but, as with these, it is easily understood by assuming a ring constitution,



or a rearrangement of some of the substances before or after saponification.

Acyl Derivatives of Methyl-o-aminophenol.

Of peculiar importance for the determination of the constitution of oxyphenylurethane and the interpretation of the nature of the diacyl derivatives of *o*-aminophenol, has been the study of the corresponding derivatives of *o*-methylaminophenol, $\text{CH}_3\text{NHC}_6\text{H}_4\text{OH}$. The replacement of one hydrogen atom by methyl made it possible to determine the seat of acidity in oxyphenylurethane and, preventing a rearrangement of the diacyl compounds, made a close study of the two isomeric series possible. The methylaminophenol necessary for the experiments, I found, can be prepared much more readily by means of carbonylmethylaminophenol than by way of the corresponding thiocarbonylmethylaminophenol.¹

Carbonylmethylaminophenol,² $\text{CH}_3\text{NC}_6\text{H}_4\text{OCO}$.—This is best

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prepared by dissolving carbonylaminophenol in methyl alcohol, in which is dissolved 1 molecule of potassium hydroxide, and heating for two hours with somewhat more than 1 molecule of methyl iodide. By this method 70 per cent of the theoretical yield was obtained and the remainder of the carbonyl body recovered. The best results were obtained by using not more than 5 grams of the carbonyl body for one experiment. It can be purified by repeated crystallization from

¹ Jour. prakt. Chem. [2], 42, 453.

² See Bender: Ber. d. chem. Ges., 19, 2269; Carbonylethylaminophenol.

ligroin. It is very soluble in most organic solvents, but insoluble in acids and alkalies. It melts at 86° .

0.2347 gram substance gave 19.3 cc. N at 19° and 741 mm. (corr.).

	Calculated for $C_8H_7NO_2$.	Found.
N	9.39	9.42

Preparation of o-Methylaminophenol, $CH_3NHC_6H_4OH$.—Four to five grams of methylcarbonylaminophenol are sealed in a tube with 15–18 cc. of concentrated hydrochloric acid and heated to 180° for one and a half hours. The contents of the tube are then evaporated to dryness. By stopping the evaporation just at the right point, crystals of the hydrochloride can be obtained, but generally there remains a thick, sticky mass, which gradually hardens. By neutralizing this with a solution of sodium carbonate the free base, methyl-*o*-aminophenol, is liberated, as a white solid, in a fairly pure condition, and melts at 88° – 90° .¹ The base turns brown on standing in the air, especially when moist.

Benzoylmethyl-o-aminophenol, $C_6H_5CO(NCH_3)C_6H_4OH$.—3.7 grams (2 mols.) of methyl-*o*-aminophenol are suspended in ether and 2.1 grams (1 mol.) of benzoyl chloride added. After shaking for some time, the ether solution is washed and partly evaporated. Crystals are deposited, which, after two recrystallizations from alcohol, melt at 160° – 162° . The compound was dried at 105° and analyzed.

0.2845 gram substance gave 15.9 cc. N at 17° .5 C. and 727.5 mm. (corr.).

	Calculated for $C_{14}H_{13}NO_2$.	Found.
N	6.16	6.31

The substance is soluble in alkali and is reprecipitated by acids.

Benzoylmethyl-o-aminophenylethyl Carbonate, $C_6H_5CON(CH_3)C_6H_4OCO_2C_2H_5$.—4.5 grams of benzoylmethyl-*o*-aminophenol were dissolved in 1 molecule of potassium hydroxide, and then a little more than 1 molecule of ethyl chlorformate added. A semisolid substance separated. This was extracted with ether, and the ether solution washed and

¹ Seidel gives m. p. 80° . See J. prakt. Chem. [2], 42, 453.

dried. On evaporating the ether an oily, crystalline mass was deposited, which was exceedingly soluble in alcohol, ether, and benzene, fairly soluble in ligroin (40° – 60°). From the last solvent long, silky needles, free from oil and melting at 68° , were obtained.

0.3419 gram substance gave 14.4 cc. N at 18° .5 and 736.9 mm. (corr.).

	Calculated for $C_{17}H_{17}NO_4$.	Found.
N	4.68	4.80

One and nine-tenths grams of the substance (not quite c. p.) were shaken one and a half hours with 2 molecules of caustic soda. When nearly all had dissolved it was shaken with ether, to remove any unchanged material, then acidified and again extracted. The ether solution was washed with sodium bicarbonate. On evaporating the ether and recrystallizing the residue from alcohol it melted at 160° – 162° , and was identical with benzoylmethyl-*o*-aminophenol. The solution in bicarbonate contained a very small amount of a solid which was not identified.

o-Oxyphenylmethylurethane (ethyl-*o*-oxyphenylmethylcarbamate), $\text{HOC}_6\text{H}_4\text{N}(\text{CH}_3)\text{CO}_2\text{C}_2\text{H}_5$,—2.72 grams (2 mols.) of methyl-*o*-aminophenol were suspended in absolute ether; to this was added 1.28 grams (1 mol.) of ethyl chlorformate, and then the mixture was shaken for some time. The ether solution was poured from the hydrochloride of the base, washed, dried, and the ether evaporated. The resulting oil was distilled at reduced pressure (18–20 mm.), nearly all passing over at 175° – 180° . The oil did not crystallize in a freezing-mixture of ice and salt, nor on standing a week *in vacuo* in an ice chest. Some months later, when the temperature was -20° to -30° , it was kept for twenty-four hours at this temperature after adding a little ligroin, and thus it was crystallized. On recrystallization it tended to become oily, but I was able, by inoculation, to get a product sufficiently pure to determine the melting-point as 53° . The oil is soluble in alkalis and is reprecipitated by acids. It is separated from a little methylcarbonylaminophenol, formed in distilling, by dissolving in alkali, extracting with ether, acidifying, and again extracting. It was analyzed in the form of its benzoate.

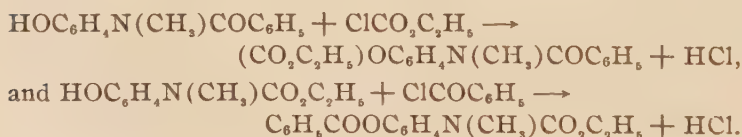
Benzoyl-o-oxyphenylmethylurethane,
 $C_6H_5COOC_6H_4N(CH_3)CO_2C_2H_5$.—The purified oil was dissolved in sodium hydroxide, 1 molecule of benzoyl chloride added, and the whole shaken for some time. A solid separated, which was purified by recrystallization from alcohol. It melted at $88^\circ-90^\circ$.

0.2623 gram substance gave 11.2 cc. N at 18° C. and 725.6 mm. (corr.).

	Calculated for $C_{17}H_{17}NO_4$.	Found.
N	4.68	4.79

The substance crystallizes in nearly white needles, is fairly soluble in most organic solvents, but insoluble in alkalis and acids.

The benzoate, saponified and treated as usual, gave benzoic acid (m. p. 121° , not depressed by an admixture of the acid), and an oil which had all the properties of oxyphenylmethylurethane. The two reactions, between ethyl chlorformate and benzoylmethylaminophenol on the one hand, and between benzoyl chloride and oxyphenylmethylurethane on the other hand, led to two different substances—stable isomers:



By saponification each compound loses first the acyl bound to oxygen. A mixture of the two isomers (melting respectively at 68° and $88^\circ-90^\circ$) had, of course, no constant melting-point, but it melted partly at 58° , and from this slowly to 80° . The former was much the more soluble in alcohol, and the general appearance of the two was quite different.

m-Nitrobenzoylmethyl-o-aminophenol,
 $HOC_6H_4N(CH_3)COC_6H_4NO_2$, was prepared from methyl-*o*-aminophenol (2 mols.) and *m*-nitrobenzoyl chloride (1 mol.). The substance is not very soluble in ether. On crystallizing from alcohol beautiful, large, nearly white crystals separated. They melted at 105° , and decomposed at $110^\circ-115^\circ$. The sub-

stance is soluble in alkalis. It was analyzed in the form of its benzoate.

m-Nitrobenzoylmethyl-*o*-aminophenol, $\text{HOC}_6\text{H}_4\text{N}(\text{CH}_3)\text{COC}_6\text{H}_4\text{NO}_2$ (1.5 grams), was dissolved in sodium hydroxide and somewhat more than 1 molecule of benzoyl chloride added. An oil separated, which solidified with difficulty. On recrystallizing it from alcohol, the crystals were pure white and exceptionally perfect, melting at 141° .

0.3231 gram substance gave 0.7908 gram CO_2 , and 0.1227 gram H_2O .

	Calculated for $\text{C}_{17}\text{H}_{16}\text{N}_2\text{O}_6$.	Found.
C	67.00	66.76
H	4.25	4.21

One gram of the substance was saponified exactly as in the former cases. The acid part melted at 117° – 120° , and, mixed with benzoic acid, this melting-point was not depressed. It also had the odor and other properties of benzoic acid. The other portion, crystallized from ether, melted at 105° and decomposed at 110° . It had all the properties of *m*-nitrobenzoylmethyl-*o*-aminophenol.

m-Nitrobenzoate of Benzoylmethyl-*o*-aminophenol, $\text{NO}_2\text{C}_6\text{H}_4\text{COOC}_6\text{H}_4\text{N}(\text{CH}_3)\text{COC}_6\text{H}_5$.--Benzoylmethyl-*o*-aminophenol, $\text{HOC}_6\text{H}_4\text{N}(\text{CH}_3)\text{COC}_6\text{H}_5$ (1.75 grams), was dissolved in sodium hydroxide (1 mol.) and *m*-nitrobenzoyl chloride (1 mol.) added. An oil separated which slowly solidified. On recrystallizing it from alcohol, it separated in large, stout crystals melting at $123^\circ.5$.

0.2109 gram substance gave 14.5 cc. N at $20^\circ.5$ C. and 735 mm.

	Calculated for $\text{C}_{21}\text{H}_{16}\text{N}_2\text{O}_6$.	Found.
N	7.45	7.78

The substance is quite soluble in alcohol, ether, and benzene; insoluble in acids and alkalis.

One gram of the substance was saponified, two to three times the calculated amount of alcoholic potash being used. All dissolved in a few minutes, and nothing was precipitated on adding water. The solution was then acidified and treated as in other cases, when it yielded benzoylmethyl-*o*-aminophe-

nol, melting at 159° – 161° , and *m*-nitrobenzoic acid, melting at 139° – 141° . A mixture of the two isomers, melting respectively at $123^{\circ}.5$ and 141° , melted at 115° . In the diacyl derivatives of methyl-*o*-aminophenol, therefore, there is no molecular rearrangement. Both isomers are stable, and by saponification the acyl attached to oxygen is always split off first.

Methylation of Oxyphenylurethane, $\text{HOC}_6\text{H}_4\text{NHCOOC}_2\text{H}_5$.—The behavior of the diacyl derivatives of *o*-aminophenol, and particularly of the acylated *o*-oxyphenylurethanes, showed plainly that we were dealing with derivatives of the ring form,



or with substances possessing a most remarkable tendency to rearrangement. The study of the acyl derivatives of *o*-methylaminophenol, particularly of *o*-oxyphenylmethylurethane, on the other hand, made the ring constitution again improbable, and the probability of molecular rearrangements correspondingly greater. As no definite conclusion as to the constitution of oxyphenylurethane was reached by this line of experiment, recourse was had again to the surer process of methylation. It had failed early in the course of this study, before the investigation of the acyl derivatives had been taken up. The failure of the earlier attempts at methylating oxyphenylurethane seemed to be due to the fact that methyl iodide, in boiling alkaline solution, reacted much too slowly to be of value in the determination of such a delicate question of constitution, and that no silver salt could be prepared on account of the sensitiveness of the substance toward silver oxide. By using Von Pechmann's method of methylating by means of diazomethane, perfectly definite results were obtained, oxyphenylurethane giving *o*-methoxyphenylurethane (anisidineurethane), $\text{CH}_3\text{OC}_6\text{H}_4\text{NHCOOC}_2\text{H}_5$, and having, therefore, the constitution $\text{HOC}_6\text{H}_4\text{NHCOOC}_2\text{H}_5$.

Since it seemed possible that *o*-anisidineurethane would be obtained, it was thought best to prepare this substance first, synthetically, from *o*-anisidine to determine the best means of identifying it. These derivatives of anisidine will be described first.

o-Methoxyphenylurethane (*o*-Anisidineurethane),

$\text{CH}_3\text{OC}_6\text{H}_4\text{NHCO}_2\text{C}_2\text{H}_5$.—Anisidine was suspended in water, an excess of alkali added, and then one molecule of ethyl chlorformate. An oil was formed, insoluble in acids. It was washed with dilute acid, extracted with ether, and this solution dried. After evaporating the ether the oil was distilled at 25–30 mm. pressure. This distillate was fractionated, when a nearly colorless oil, boiling at 180°–182° under 26 mm pressure, was obtained.

0.3146 gram substance gave 20.4 cc. N at 18°.5 C. and 733.1 mm. (corr.).

	Calculated for $\text{C}_{10}\text{H}_{13}\text{NO}_3$.	Found.
N	7.18	7.36

o-Methoxybromophenylethylurethane,

$\text{CH}_3\text{OC}_6\text{H}_3\text{BrNHCO}_2\text{C}_2\text{H}_5$.—An attempt to brominate the urethane, so as to get a solid derivative, showed that mixtures of two products were formed, one melting at 252°, the other at 102°.5, which it was very hard to purify. The last substance gave figures which corresponded very well with a monobrom derivative of anisidineurethane, but the mixtures were so difficult of separation that it was not thought practical to attempt an identification of anisidineurethane by this method. The substance, melting at 102°.5, was dried over sulphuric acid *in vacuo* and analyzed.

I. 0.2302 gram substance gave 0.3796 gram CO_2 , and 0.0997 gram H_2O .

II. 0.3181 gram substance gave 0.5211 gram CO_2 , and 0.1298 gram H_2O .

III. 0.1588 gram substance gave 0.2626 gram CO_2 , and 0.0652 gram H_2O .

IV. 0.2740 gram substance gave 12.9 cc. N at 18°.5 and 745.4 mm. (corr.).

	Calculated for $\text{C}_{10}\text{H}_{12}\text{BrNO}_3$.	I.	II.	Found. III.	IV.
C	43.79	44.96	44.67	45.08	
H	4.37	4.82	4.52	4.53	
N	5.10				5.43

A much more satisfactory identification was based on the change of the urethane into the corresponding urea chloride

by means of phosphorus pentachloride, according to the method of Lengfeld and Stieglitz,¹ as modified by Folin and Stieglitz. The urea chloride was converted into anisidine-urea and anisidinephenylurea, which were easily purified and identified. The reactions are represented thus:



Two and two-tenths grams of anisidineurethane were placed in a distilling flask, and after adding some chloroform and 2.33 grams (1 mol.) of phosphorus pentachloride the mixture was warmed on a water-bath to 50°–55° as long as a gas (ethyl chloride) was evolved. Then the contents of the flask were cooled and dry hydrogen chloride passed through the solution until the chloroform and most of the phosphorus oxychloride were evaporated. More chloroform was added and again evaporated. Without attempting to purify the urea chloride it was converted into the urea by pouring it into a concentrated solution of ammonia. Immediately an amorphous solid, which was very soluble in alcohol, separated, but on adding water to the alcoholic solution a crystalline substance, which melted at 130°–140°, separated. On boiling it with ligroin, in which it was insoluble, then recrystallizing it from water again, and finally from chloroform and ligroin, the melting-point became constant at 143°–145° (Beilstein gives m. p. 146°.5). It was identical with the urea made from anisidine hydrochloride and potassium isocyanate.

o-Anisidinephenylurea, $(\text{CH}_3\text{O})\text{C}_6\text{H}_4\text{NHCONHC}_6\text{H}_5$.—0.61 gram of anisidine and 0.59 gram of phenyl isocyanate were mixed in a small beaker, cooled with water. On stirring the mass a thick, heavy oil formed. When the reaction was ended dilute hydrochloric acid was added, which caused the oil to solidify. The urea is soluble in alcohol, ether, and chloroform, almost insoluble in ligroin (40°–60°). Recrystallized from alcohol, it melts at 144°. Dissolved in chloro-

¹ This JOURNAL, 16, 70.

form and precipitated with ligroin, it crystallized in thick prisms with the same melting-point.

0.2709 gram substance gave 28 cc. N at 22° and 736.8 mm. (corr.).

	Calculated for $C_{14}H_{14}N_2O_2$.	Found.
N	11.66	11.65

On heating a little on platinum foil a strong odor of isocyanate was noticed.

The urea chloride of anisidine was again made, as before described, from the urethane, and then poured into an excess of pure aniline. A heavy, thick oil formed, mixed with a solid. It was washed with dilute acid and water, the oil extracted with ether, and the ether evaporated. The thick oil which remained refused to crystallize even when scratched with a glass rod, and allowed to stand *in vacuo* for several days. But on rubbing into the oil, moistened with alcohol, a crystal of the synthetic urea, it became crystalline immediately. It was recrystallized from alcohol, then from chloroform and ligroin. The crystals now softened at 141° and melted at 142°–144°. Mixed with the synthetic urea the point of fusion was raised slightly. When heated on platinum foil the isocyanate odor became distinctly perceptible.

Methylation of o-Oxyphenylurethane with Diazomethane.—

The diazomethane was prepared from nitrosomethylurethane according to the method of Von Pechmann.¹ The methylamine was prepared from acetamide² according to Hofmann's method. Nitrosomethylurethane was prepared by following the description of Von Pechmann,³ the ethereal solution of the urethane being placed in the separating-funnel in which it was to be washed and dried. In this way I avoided entirely the disagreeable effects experienced by this experimenter.

One and eight-tenths grams of oxyphenylurethane were

¹ Ber. d. chem. Ges., 28, 855.

² As no details could be found of the methods employed for making acetamide from ammonia and acetic ether, experiments were carried out to determine the conditions for obtaining the best yield. By mixing 100 grams of the ether with 200 cc. of concentrated ammonia (sp. gr. 0.90), and allowing the mixture to stand until it had become homogeneous (two days), and then distilling, 75–80 per cent of the theoretical amount was obtained.

³ Loc. cit.

dissolved in a small amount of ether, and to this solution was added diazomethane dissolved in ether. The whole was then warmed on the water-bath for an hour, a reflux condenser being used. The yellow color of the solution nearly disappeared and a gas (nitrogen) was evolved. More diazomethane was added and it was again warmed. When the color of the solution remained light-yellow, which showed a slight excess of diazomethane, the ether solution was washed with sodium hydroxide, then with hydrochloric acid and water. On drying and evaporating the ether an oil remained, insoluble in acids and alkalis. It is somewhat viscous, possesses a pleasant, ethereal odor, and is soluble in most of the organic solvents. It could not be made to crystallize in the cold, but was identified as *o*-methoxyphenylethylurethane,



by converting it into methoxyphenylurea and methoxycarbonylanilide by treatment with phosphorus pentachloride, followed by ammonia or aniline, as described above for the synthetic urethane. 0.7 gram of the urethane was thus converted into the urea. A little oil separated, which soon solidified. After filtering it off the solution was evaporated to dryness. The solid residue was dissolved in chloroform, and ligroin carefully added. Transparent crystals formed which, after several recrystallizations, were of a light-brown color, and melted at 145° , softening a little at 140° – 142° . Mixed with the urea (m. p. 143° – 145°) made from anisidine urethane, the melting-point was not depressed. The crystal forms, as seen under the microscope, were the same, proving conclusively that the two substances are identical.

More of the urea chloride of the methylated urethane was made as already described, and poured into an excess of aniline. A thick oil was formed, which was washed with dilute acids and water. On rubbing the oil with a crystal of the synthetic urea it became a solid mass of crystals. These were purified by recrystallizing from chloroform and ligroin. The substance melted at 144° , and, mixed with the synthetic phenylurea, the melting-point was not depressed. On heating some of the substance on platinum foil, the isocyanate

odor was easily perceptible. The methylated oxyphenylurethane is undoubtedly an anisidine derivative, and therefore *o*-oxyphenylurethane must contain a phenol hydroxyl group.

o-Aminophenylethyl Carbonate, $\text{H}_2\text{NC}_6\text{H}_4\text{OCO}_2\text{C}_2\text{H}_5$.—Having established the fact that a rearrangement occurs when *o*-nitrophenyl carbonate is reduced with tin and hydrochloric acid, and that oxyphenylurethane was the only product thus far liberated, it seemed of interest to isolate the free aminophenyl carbonate, which must be the first product of the reduction, as that might throw some light on the mechanism of the rearrangement. After some unsuccessful attempts, the following method was found to give satisfactory results:

Four grams of *o*-nitrophenyl carbonate are put in a flask with 15 cc. of concentrated hydrochloric acid and cooled in ice-water. To this is added powdered tin in small portions and the whole shaken, the temperature being kept near 0° . If the solution is kept sufficiently cold, almost immediately after becoming clear a fine, white, crystalline solid begins to appear. This contains both organic and inorganic material and is probably a double salt. When no more crystals form, the contents of the flask are poured slowly into a well-cooled solution of 50 grams of potassium hydroxide in 50 cc. of water. If too much heat is allowed to develop at this stage the results are negative. The alkaline solution is immediately extracted six times with ether, a sufficient amount of water being added during the last extractions to dissolve the potassium chloride. The ether solution is washed with water and then dried with solid potassium hydroxide. When dry, the ether is poured off and dry hydrogen chloride passed into it. A copious, white precipitate of the hydrochloride of *o*-aminophenylethyl carbonate is formed which can be filtered and dried on a clay plate. It is stable at the ordinary temperature, and remains perfectly white. From 60–70 per cent of the theoretical yield is obtained. It melts at 150° – 152° with evolution of much gas. It is very soluble in cold water and in alcohol. Sodium carbonate decomposes it, forming aminophenylethyl carbonate, an oil which is soluble in dilute acids. On heating an aqueous solution of the salt it becomes cloudy

before the boiling-point is reached, and an oil separates which gradually solidifies on cooling. On recrystallizing this solid from somewhat diluted alcohol, crystals are formed which melt at 85° – $86^{\circ}.5$, and resemble oxyphenylurethane. When these crystals are mixed with oxyphenylurethane the melting-point is not depressed. It is also soluble in alkalies and is reprecipitated by acids. A nearly saturated solution of the hydrochloride of *o*-aminophenylethyl carbonate was made, and to this a concentrated solution of platinic chloride was added. After a few minutes, yellow crystals formed. They were somewhat soluble in water and alcohol, insoluble in ether. They were washed with ether in which was some alcohol, dried and analyzed.

0.0446 gram chlorplatinate gave 0.01125 gram of platinum.

	Calculated for $C_{18}H_{24}N_2O_6PtCl_6$.	Found.
Pt	25.16	25.22

0.1664 gram of the hydrochloride was titrated with tenth-normal silver nitrate, potassium chromate being used as indicator. 7.7 cc. of the solution were required.

	Calculated for $C_9H_{12}NClO_3$.	Found.
Cl	16.32	16.42

Some of the salt was put into a separating-funnel with ether and a solution of sodium carbonate added to alkaline reaction. The ether solution was then washed, dried with fused potassium sulphate, and the ether evaporated *in vacuo*. Aminophenylethyl carbonate remained as a basic oil, which was easily soluble in dilute acids and could be converted back into the hydrochloride and the chlorplatinate of *o*-aminophenylethyl carbonate. It was kept over sulphuric acid. After twelve hours it had changed to a crystalline solid which melted at 86° , and it was now soluble in alkalies and was reprecipitated by acids. All the properties of this solid, as well as the melting-point of a mixture with oxyphenylurethane, proved it to be this substance.

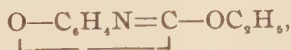
In an attempt to convert the hydrochloride of aminophenylethyl carbonate into the corresponding urea, 0.3 gram of the hydrochloride was dissolved in water and a solution of potas-

sium isocyanate added. An oil separated which was dissolved in water, and, on standing some hours, crystals melting at 86° separated, which proved to be oxyphenylurethane. Another attempt was made, an alcoholic solution of the salt being used, but it was converted into the urethane, as in the former experiment. Evidently the rearrangement takes place rather than the usual addition to isocyanic acid.

One gram of the hydrochloride was treated with an ice-cold solution of 2 molecules of sodium hydroxide and a little more than 1 molecule of benzoyl chloride added. The solution was then extracted with ether several times. The residue, left on evaporating the ether, was again digested with very little ether, which dissolved all but a little, and this, recrystallized from alcohol, melted at 180° , and, mixed with dibenzoylaminophenol, did not melt lower.¹ The ether solution deposited crystals which, after one recrystallization from ligroin, melted at 76° and in its crystal form as in its other properties, was identical with the benzoyl derivative of oxyphenylurethane. A mixture of the two had the same melting-point.

In a second attempt to prepare the isomer of the latter compound a little more than 1 gram of the hydrochloride, corresponding to 0.9 gram (2 mols.) of the free base, was put in a separating-funnel with ether and then treated with an excess of sodium carbonate. The ether solution of the free base was washed, dried with solid potassium hydroxide, and then 1 molecule of benzoyl chloride added. After a minute the hydrochloride of 1 molecule of the base separated. This was filtered out, the ether washed with alkali, then with dilute acid, finally with water, and dried with calcium chloride. On distilling the ether a solid remained which melted at 76° . Mixed with the benzoyl derivative of oxyphenylurethane, the melting-point was not depressed.

In order to compare the behavior of aminophenylethyl carbonate towards dilute acid, with that of ethoxymethenylaminophenol,



¹ Hübner gives 176° as the melting-point of this derivative.

1 gram of the hydrochloride was allowed to stand twenty-four hours with less dilute hydrochloric acid than was sufficient to dissolve all of it. Then it was completely dissolved in this reagent. After standing some days longer, the solution was divided into two portions and one was extracted with ether. On evaporating the ether a solid remained, which, after one recrystallization from water, melted at 70° – 119° . The other portion, on standing longer, deposited crystals which melted at 70° – 80° , but when mixed with oxyphenylurethane, the melting-point was raised a little. Decomposing this by distilling some of it into the upper part of a test-tube the melting-point was raised to 135° – 137° , which proved the sublimate to be carbonylamino-phenol. It is quite certain that the original product is a mixture of oxyphenylurethane and carbonylamino-phenol, as I have found that mixtures of these, in different proportions, have melting-points anywhere between 70° and 120° . By distillation they give pure carbonylamino-phenol.

Action of Hydrochloric Acid on Ethoxymethenyl-o-aminophenol.

—In the reduction of the *o*-nitrophenyl carbonate it was thought possible that the hydrochloride of the anhydro base, ethoxymethenylaminophenol, might be formed¹ instead of the amino base. A comparison of this base with aminophenyl-ethyl carbonate was, therefore, undertaken. Some of the anhydro base, obtained through the kindness of Dr. H. N. McCoy, was dissolved in absolute ether and dry hydrogen chloride passed into the solution. The first bubbles produced a crystalline deposit, but this immediately disappeared, and, on evaporating the ether, only carbonylamino-phenol remained. The experiment was repeated in dry ligroin solution at -11° . A solid separated which was stable at that temperature, but when put on a clay plate in a cold room the crystals began to decompose, giving off a gas (ethyl chloride) which burned with a green flame. On the clay plate there remained pure carbonylamino-phenol (m. p. 136° – 138°).² The behavior of this

¹ As in Böttcher's experiments with *o*-nitrophenylbenzoate.

² This is the typical behavior of the hydrochloride of an imido ether which ethoxymethenylaminophenol hydrochloride represents:



Attention may be called to the unusually low temperature at which the salt decom

base is therefore different from that of the amino base formed by reducing *o*-nitrophenyl carbonate. And this fact, coupled with the observation already given, that the amino base on standing is converted into the urethane while the anhydro base is stable in ordinary moist air, proves conclusively that the latter is not an intermediate product in the intramolecular rearrangement.

For reasons stated in the introduction (p. 11), it was thought desirable to compare the behavior of the anhydro base toward dilute hydrochloric acid with that of aminophenylethyl carbonate (see above). The anhydro base was allowed to stand several days in contact with dilute hydrochloric acid. The oil gradually disappeared and was replaced by white crystals. When all the oil had disappeared the crystals were filtered off, recrystallized from water, and dried. They melted at 70°–80°, were soluble in alkali, and reprecipitated by acids. On distilling into the upper part of a test-tube and then recrystallizing from water, in which was a little alcohol, a substance melting at 136°–138° was obtained, which proved to be carbonylaminophenol. The low-melting substance is certainly a mixture of oxyphenylurethane, and carbonylaminophenol. The products formed are identical with those obtained by allowing the hydrochloride of aminophenyl carbonate to stand in an acid solution.

p-Nitrophenyl Carbonate, $\text{NO}_2\text{C}_6\text{H}_4\text{OCOOC}_2\text{H}_5$.—The peculiar rearrangement observed on reducing *o*-nitrophenyl carbonate in the usual way, by which *o*-oxyphenylurethane results, suggests a comparison of corresponding derivatives in the meta or para series, preferably the para series, as that is the more susceptible to molecular rearrangement, and usually resembles the ortho series more than the meta series does.

Ten grams of *p*-nitrophenol were treated with excess of potassium hydroxide, and somewhat more than 1 molecule of poses. It recalls the behavior of the hydrochloride of ethylphenylimidochlorformate, $\text{ClC}(\text{NC}_6\text{H}_5)\text{OC}_2\text{H}_5$, which, decomposing below –15° into ethyl chloride and chlorformanilide, could not be isolated by Lengfeld and Stieglitz,¹ although its formation was clearly indicated and formed an important link in their arguments. The properties of the solid hydrochloride of ethoxymethenylaminophenol fully support their assumption of such an intermediate hydrochloride.

¹ Am. Chem. J., 16, 73.

ethyl chlorformate was added in small portions, while the contents were vigorously shaken. A quantitative yield of a nearly white solid melting at 68° was obtained.

0.2533 gram substance gave 14.8 cc. N at 17° and 736.8 mm.

	Calculated for $C_9H_9NO_5$.	Found.
N	6.63	6.71

The carbonate is soluble in ligroin, ether, alcohol, and somewhat in boiling water, from all of which it crystallizes in long, white needles.

Synthesis of p-Nitrophenylethyl Carbonate.

In order fully to establish that in *p*-nitrophenyl carbonate the carbethoxy group is attached to phenol oxygen and not to the nitro group, a synthesis from phenylethyl carbonate was carried out. The phenyl carbonate was cooled to 0° in ice-water and then poured slowly into ice-cold, fuming nitric acid. On pouring the mixture into water a nearly white, crystalline solid separated immediately. If allowed to stand for some time in the strong nitric acid the product is much more impure. On recrystallizing from alcohol it crystallizes well and melts at 68° . A mixture of this with the carbonate made from *p*-nitrophenol has the same melting-point as either, and the two are identical in all their properties.

p-Aminophenylethyl Carbonate, $H_2NC_6H_4OCO_2C_2H_5$.—Several attempts were made to reduce the carbonate with tin and hydrochloric acid, in aqueous and in alcoholic solution, but the yields in each case were small owing to the fact, afterwards discovered, that the base is somewhat soluble in water and is not extracted with ether completely. The best results are secured by proceeding as follows :

Two grams of the nitrocarbonate were dissolved in warm alcohol, concentrated hydrochloric acid added, and then slowly, and in small portions, 11 grams (6 mols.) of stannous chloride. The solution became light-yellow. After fifteen minutes a drop gave no precipitate with water. The whole was then diluted and hydrogen sulphide passed into the solution, until all the tin was thrown down. After filtering, the solution was concentrated *in vacuo* at 50° – 55° . On standing,

white crystals of the hydrochloride of *p*-aminophenylethyl carbonate were deposited. The yield was 70 per cent. The crystals are very soluble in water. From dilute solutions caustic alkalies do not precipitate the base. From fairly concentrated solutions sodium hydroxide or sodium carbonate precipitates an oil which solidifies on standing and then melts at 36°. On recrystallizing it an oil, which solidifies only on standing some days, is formed at first. Both crystals and oil dissolve in acid. The base is somewhat soluble in water, gives no purple color with ferric chloride, and does not become colored in the air. On heating the hydrochloride it darkens at 160° and melts at 197° with violent decomposition.

0.2005 gram of the hydrochloride dissolved in water and titrated with tenth-normal silver nitrate, potassium chromate being used as indicator, required 9.3 cc. of the nitrate solution.

	Calculated for $C_9H_{12}NO_3Cl$.	Found.
Cl	16.32	16.46

The platinum salt was made in aqueous solution by precipitating with chlorplatinic acid, washing the precipitate with alcohol and ether, and then drying *in vacuo* over sulphuric acid.

0.2869 gram substance gave 0.0722 gram Pt.

	Calculated for $(C_9H_{12}NO_3)_2PtCl_6$.	Found.
Pt	25.16	25.16

It is a bright-yellow, crystalline solid melting at 237°, blackening at 208°.

p-Ureidophenylethyl Carbonate, $NH_2CONHC_6H_4OCOOC_2H_5$.
—The paraminophenylethyl carbonate can also be identified easily by converting it into its urea. 0.3 gram of the hydrochloride was dissolved in a little water and the calculated amount of potassium cyanate added. An oil separated which soon became crystalline. On crystallizing once from hot water it was nearly white and melted at 147°–150°. It is insoluble in alkalies.

All attempts to cause a rearrangement of *p*-aminophenylethyl carbonate to *p*-oxyphenylurethane were unsuccessful. One gram of the hydrochloride was dissolved in water, and,

after the addition of some hydrochloric acid, the solution was allowed to stand two days. No change having taken place, apparently, the solution was boiled two and a half hours under a reflex condenser. It was then allowed to stand a week. The solution was then evaporated at 50° – 60° *in vacuo* in an atmosphere of hydrogen sulphide. The residue was washed with a little water, filtered, and tested as follows:

Ferric chloride produced a deep-purple color, due to *p*-aminophenol. Sodium carbonate produced a solid which gradually turned brown on standing. A urea, made as in the former experiment, melted at 167° , blackening at 162° (*p*-oxyphenylurea melts at 167°). It was quite soluble in alkalies. Mixed with the urea of *p*-aminophenyl carbonate (m. p. 147° – 150°), the melting-point became 130° – 150° . Evidently the acid had caused a saponification of the hydrochloride of *p*-aminophenylethyl carbonate to that of *p*-aminophenol.

Another gram of the hydrochloride of *p*-aminophenylethyl carbonate was dissolved in water and allowed to stand at the temperature of the room for a week. The solution was then evaporated as was the first portion. Ferric chloride gave a very light-purple color. Sodium carbonate precipitated an oil which became solid on inoculating it with a crystal of *p*-aminophenyl carbonate. The oil dissolved in hydrochloric acid. The urea was made as in the former case. It softened slightly at 142° , melting at 146° – 148° . Mixed with a synthetic *p*-ureidophenylethyl carbonate, the melting-point was not lowered. It was insoluble in alkalies. No change had occurred. A third portion of the hydrochloride was dissolved in water and alcohol, allowed to stand a week, and then treated as in the former case.

Ferric chloride gave a reddish-purple color. Sodium carbonate separated an oil which gave tests corresponding to *p*-aminophenyl carbonate and formed the same urea. It is evident from these tests that *p*-aminophenylethyl carbonate exhibits no tendency to change into a urethane corresponding to *p*-oxyphenylurethane.

I wish here to express my thanks to Professor Stieglitz for valuable suggestions and for the careful attention he has given to each step of this work.

